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Brain Tumor in a Dish: Glioma/Astrocyte Co-Cultures as a Model for In Vitro Studies

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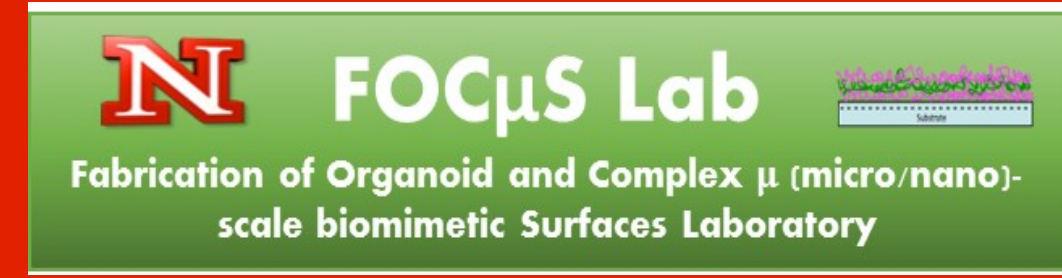
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Brain Tumor in a Dish: Glioma/Astrocyte Co-Cultures as a Model for *In Vitro* Studies



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ABSTRACT

This study seeks to engineer an in vitro co-culture model to elucidate the role of glioma-astrocyte interactions on molecular changes in the tumor microenvironment. The use of patterned co-cultures created with polyelectrolyte multilayers and micromolding in capillaries will allow the investigation of cell-cell communication. This study will lead to better understanding of the role of healthy cells in cancer progression and potential treatment options.

INTRODUCTION

Glioblastoma

- Most commonly diagnosed primary malignant brain tumor with 17,000 new diagnoses every year
- Median survival of adults with aggressive glioblastoma is 14.6 months
- Only 30% of patients live to two years
- Invades and manipulates healthy tissue increasing survival and progression

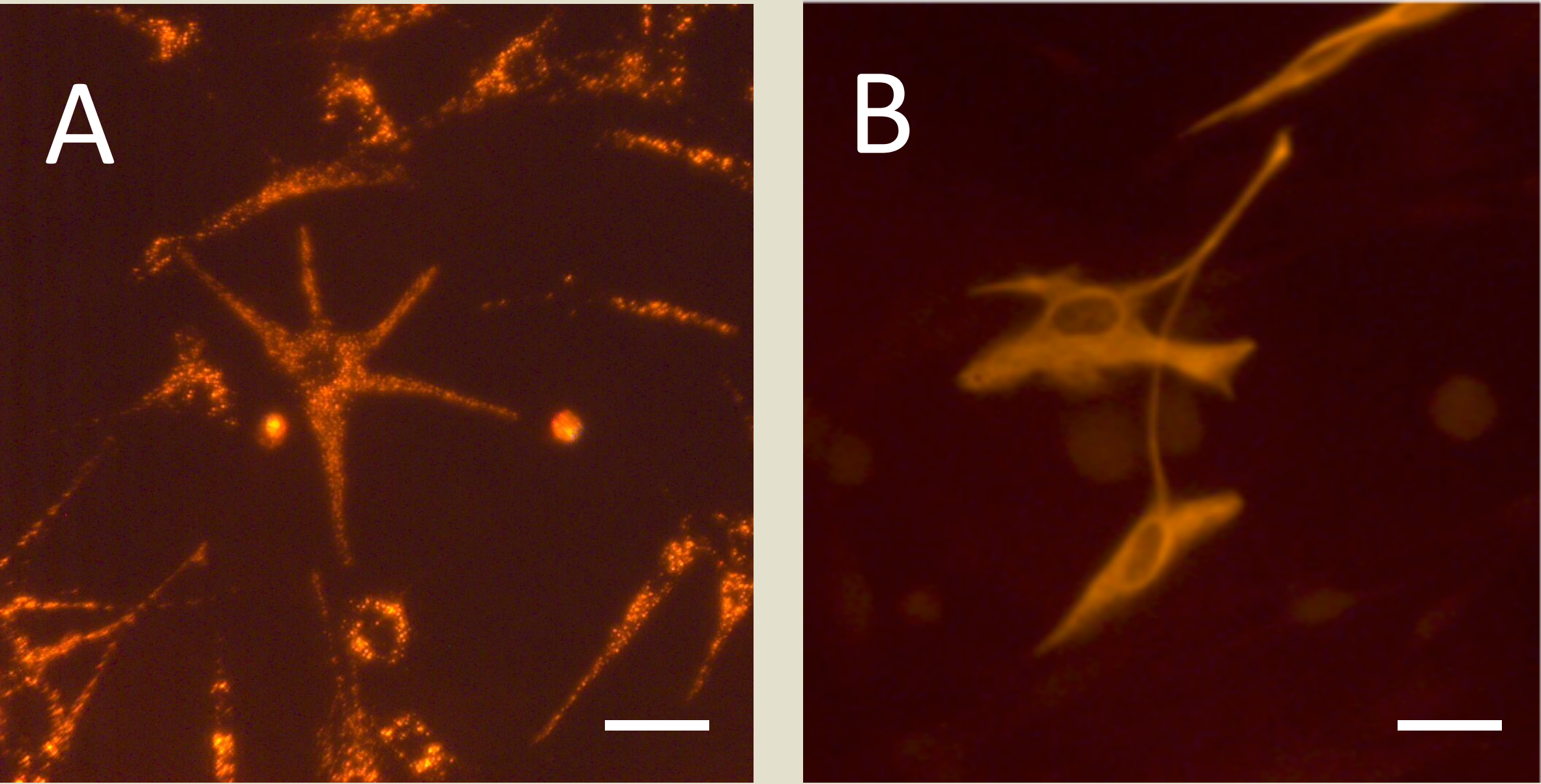


Figure 1: **A)** (left) PKH26 red dyed glioblastoma cells (A172) **B)** (right) GFAP immunostained astrocytes. (Scale Bar 100 μm)

Astrocytes

- Most abundant cell type in the brain
- Play important roles in maintenance of ion homeostasis, injury repair, and neurotransmitter recycling
- When exposed to a system injury, take on a state of altered morphology and gene/protein expression known as astrogliosis
- Astrogliosis can enhance glioblastoma malignancy by inducing aberrant cell proliferation and invasion.

Substrate Patterning for Co-culture Model

Current methods:

- Conditioned media or transwell
lack the critical component of physical contact between cells
- Random co-cultures
experiments are not reproducible

Patterned co-cultures:

- Developed using polyelectrolyte multilayers (PEM)
- Micro-molding in capillaries (μ-MC) (figure 2)
- Advantages:
 - reproducibility
 - versatility
 - low cost batch production.

Current patterned co-culture models include liver, brain, and breast cancer however to our knowledge there is no such patterned system of glioblastoma.

EXPERIMENTAL DESIGN

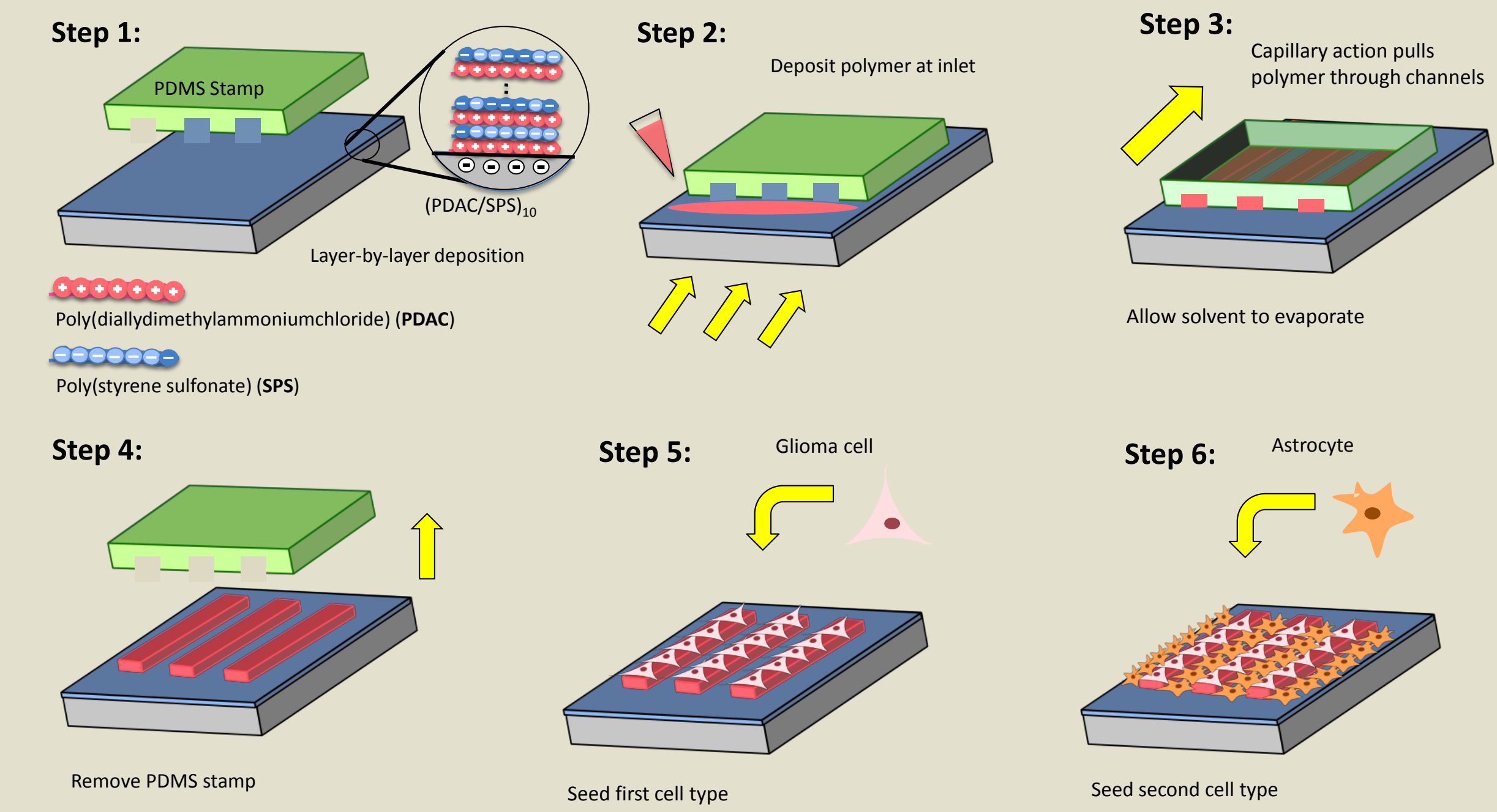


Figure 2: Schematic overview for employing PEMs and micro-molding in capillaries to create patterned co-culture platform of glioma cells and astrocytes.

DESIGN PATTERNED CO-CULTURE

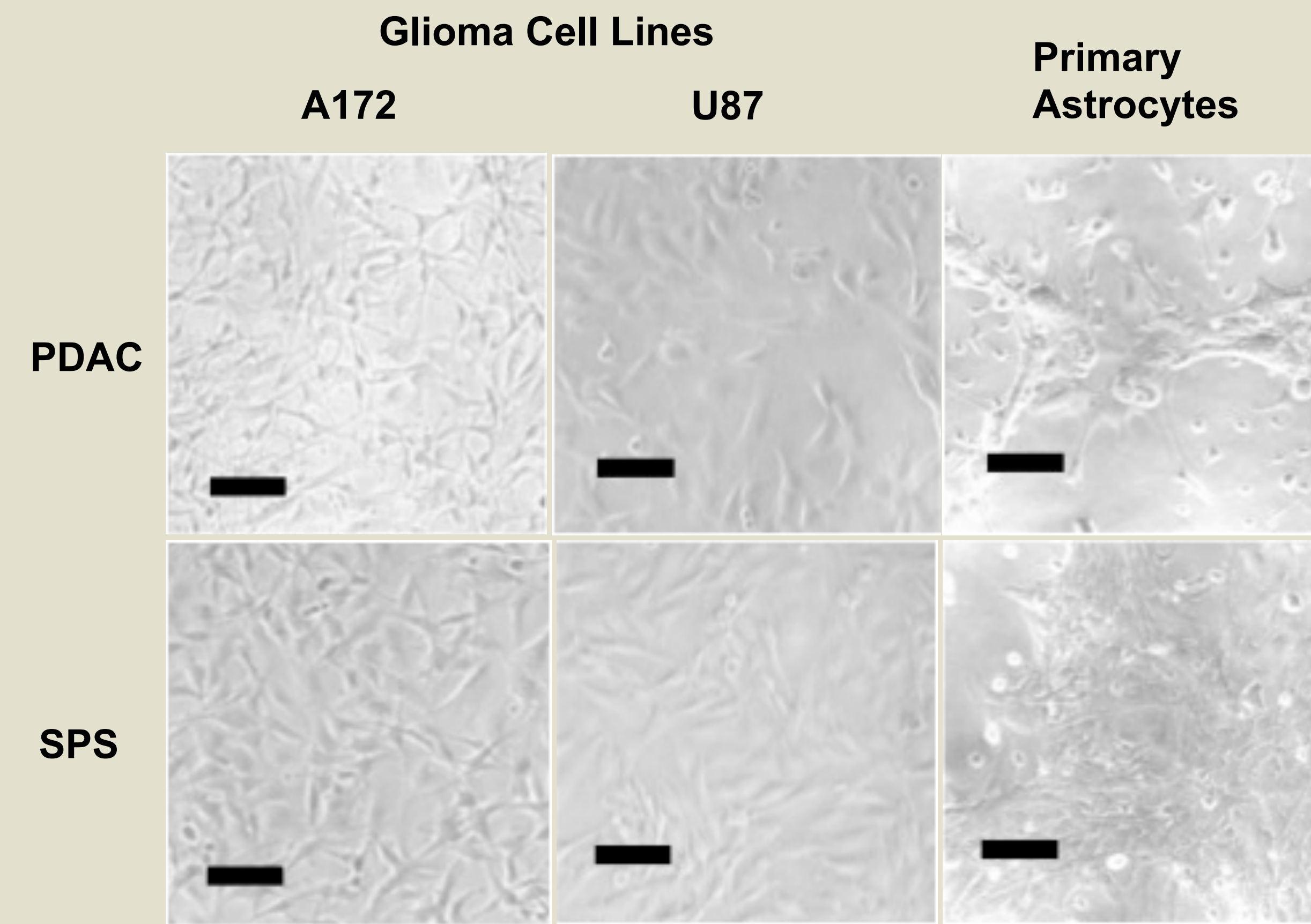


Figure 3: Phase contrast images of glioma cell lines and primary astrocytes after 3 days in culture on PEM surfaces. Top: (PDAC/SPS)10.5 – PDAC topmost surface with (from left to right) A172, U87, Astrocytes. Bottom: (PDAC/SPS)10 – SPS topmost surface with (from left to right) A172, U87, Astrocytes. (Scale Bar 100 μm)

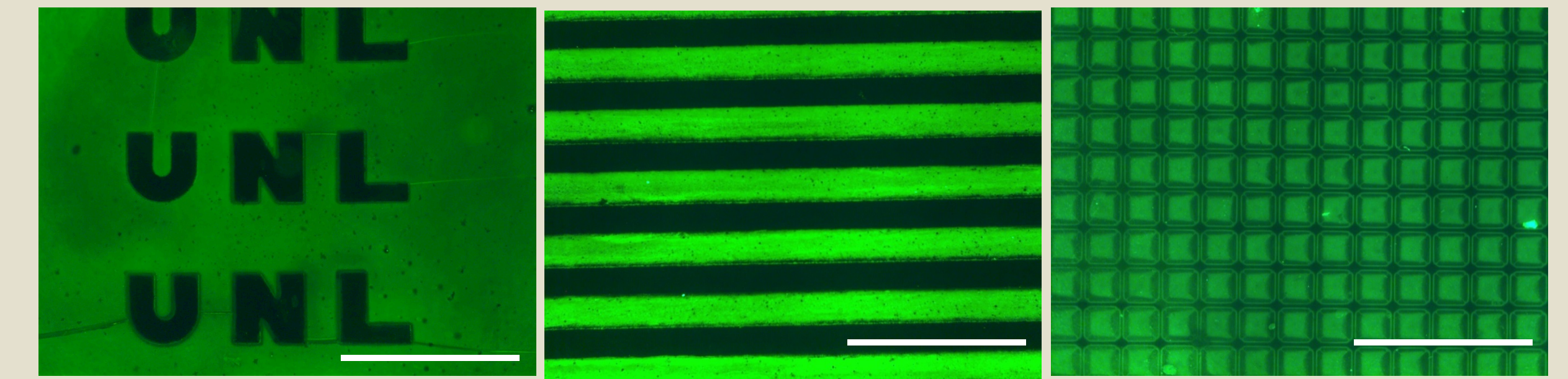


Figure 4: μ-MC of PEMs allows the investigator to adjust surface conditions (chemistry, shape, and size) to optimize culture. PEMs stained with carboxyfluorescein. (Scale Bar 1000 μm)

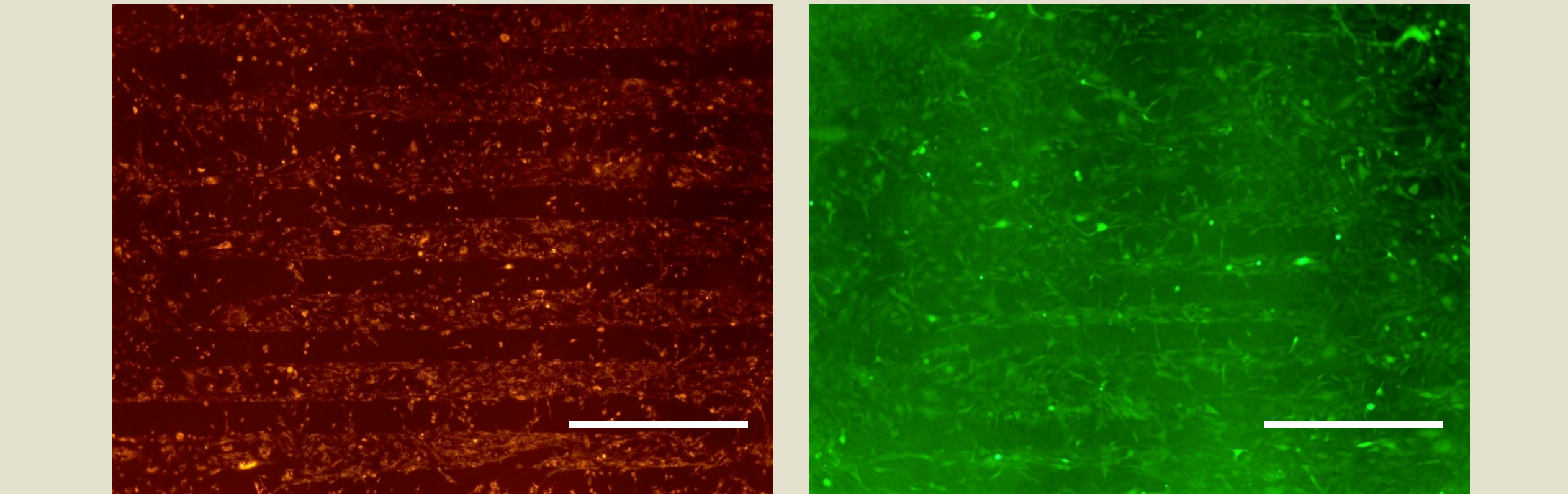


Figure 5: Patterned glioma mono-cultures on PEM patterned surfaces stained with PKH26 (red) and carboxyfluorescein (green). (Scale Bar 1000 μm)

RESULTS

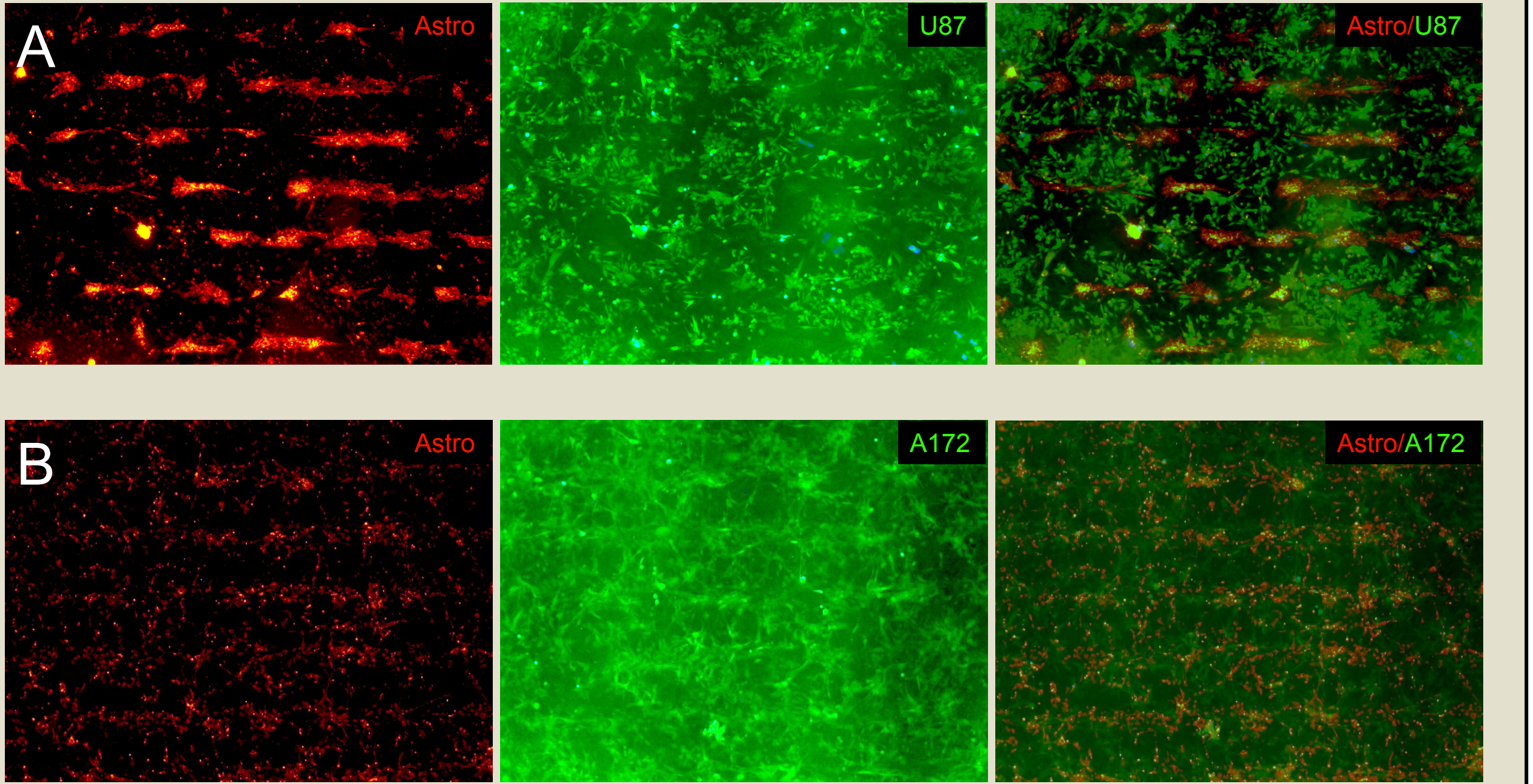


Figure 6: Fluorescent images on day 4 of co-culture. Astrocytes co-cultured with U87 glioma cells (A) and astrocytes co-cultured with A172 glioma cells (B) on day 4 of co-culture demonstrating the selective ability of our PEM surfaces.

CONCLUSIONS

Using patterned, thin polymer films creates a low cost, versatile, and reproducible co-culture that allows cell-cell contact. Patterns allow cells to attach in a controlled manner creating a platform for the study of cell-cell interaction. Future separation of co-culture will allow the study of individual cells after contact with other cells to investigate changes in cellular biochemistry.

FUTURE WORK

Future work will include optimizing the separation of the co-culture and analyzing protein expression to uncover effects of astrocytes on proliferation and metastasis of glioblastoma. From there, drug resistance studies will be done to discover the role of astrocytes in treatment resistance and find potential new treatments for glioblastoma.

REFERENCES

1. Biasoli, D., et al. "Glioblastoma cells inhibit astrocytic p53-expression favoring cancer malignancy." *Oncogenesis* 10.1038 (2014)
2. Omuro, Antonio; DeAngelis, Lisa M.; "Glioblastoma and Other Malignant Gliomas: A Clinical Review." *The Journal of the American Medical Association* 10.1001 (2013): 1842-1850
3. Kawakami, Mariko, et al. "Mutation and Functional Analysis of IL-13 Receptors in Human Malignant Glioma Cells" *Oncology Research* (2001): 459-467
4. Phuphanich, Surasak, "Glioblastoma and Malignant Astrocytoma" *American Brain Tumor Association*
5. Kidambi, Srivatsan, et al. "Patterned Co-culture of Neurons and Astrocytes on Polyelectrolyte Multilayer Films for Studying Astrocyte Mediated Oxidative Stress in Neurons" *Advanced Functional Materials* 18 (2008) 294-301
6. Kidambi, Srivatsan, et al. "Selective Adhesion of Primary Hepatocytes on Polyelectrolyte Multilayers: Template for Patterned Cell Co-culture" *Macromolecular Biosciences* 7(3) (2007) 344-53
7. Kidambi, Srivatsan, et al. "In vitro Co-cultures of Breast Cancer Cells and Stromal Cells to Emulate Tumor Progression and miRNA Profiles of Clinical Conditions" *Nature Scientific Reports* (2015)

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